

## **Choice of outcome measures for the VISION pilot trial of interventions for hemianopia.**

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No conflicting relationship exists for any author

### **Competing interests**

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Dear Editor,

We thank Bowers and colleagues for their considered comments of the VISION pilot trial results [1].

The primary queries raised by Bowers et al relate to the selection of the primary and secondary outcome measures in the VISION trial. The primary outcome was change in visual field area from baseline to 26 weeks and the secondary measures were the Rivermead Mobility Index, Visual Function Questionnaire 25/10, Nottingham Extended Activities of Daily Living, EuroQol, Short Form-12 questionnaire and Radner reading ability. The VISION trial was planned in 2009 and, based on the available evidence at that time, the choice of outcome measures was appropriate, as we explain below.

VISION trial planning preceded the publication of a Cochrane systematic review on interventions for visual field loss following stroke [2]. Thus, a literature review by the trial team in 2009 reviewed the outcome measures reported by others [e.g. 3-13]. From this review, for all studies reporting outcomes for visual scanning training, visual field assessment was the only outcome measure (as a primary or secondary outcome measure) consistently used across all studies. For studies reporting

outcomes for prism wear, all but one study [10] reported visual field assessment (with/without prism to consider field expansion effect).

As visual field assessment was consistently measured in all the key previous studies, it was an important outcome measure to consider in the VISION trial. Previous studies of interventions for hemianopia, particularly visual scanning training, had reported some apparent recovery in visual field defects (measured by visual field assessment) despite no change in objective measurements of visual field defect boundary. This was reported as being due to compensatory processes including better stimuli detection and faster reaction times to stimuli in the hemianopic field, along with unstable central fixation with eye movements towards the hemianopic side [14-17]. However there was insufficient information on the extent of variations that might occur in visual field measurements with natural adaptation (captured through the control arm) versus adaptation following different interventions (visual scanning training or prism therapy); we wished to explore this further.

Participants in the VISION trial could be recruited from 2 weeks to 6 months post stroke onset. Bowers et al correctly note that 'prior research suggests there may be spontaneous recovery of the visual field up to 3-6 months following stroke' [18,19]. Because of this, many studies recruit participants after at least 6 months post stroke onset to ensure stability of hemianopia. However, it is also known that about half of stroke survivors with hemianopia show no recovery of visual field loss [18,19] and notably there are a number of reported studies that recruited participants with hemianopia at earlier time periods [3,5,6,9]. A further advantage of measuring relative change in visual field over time was that it allowed us to explore the acknowledged risk of possible natural recovery over several time points of baseline through to 6, 12 and 26 weeks [2,14,20].

Bowers et al query the value of computing sample sizes for various minimally clinically important changes in visual field data as a basis for sample size calculations for future trials. We would agree these calculations are no longer of practical relevance. However since generating these calculations was one of the objectives of the trial, it was important to include them for completeness and to avoid reporting bias. As Bowers et al have correctly identified, we stated in our conclusions that alternative primary outcome measurement should be considered for future clinical trials. We recognise that, considering the current 2017 evidence base, other outcome measures, specifically vision- and health- related quality of life instruments are now more important.

In our pre-trial literature review, additional reported outcome measures included blind side detection rates, eye movement recordings, quality of life questionnaires, reading rates and patient perceptions of treatment, continued prism wear and participant ratings of prism helpfulness, and falls amongst others. However, none of these were used consistently across all studies. The majority of the VISION secondary outcome measures related to activities of daily living performance and quality of life instruments. A Cochrane systematic review for interventions for hemianopia [2] concluded that further trials should specifically concentrate on functional and quality

of life outcomes. Although this was published after VISION had started, we had already recognised this lack of functional outcome measures in previous studies. An objective of the pilot trial was therefore to explore quality of life and activities of daily life; appropriate measures were selected.

In the absence of consistent choice of functional activity outcome measures evident from our literature review, decisions about outcomes were made by expert stroke clinicians (physicians, occupational therapists and physiotherapists with clinical trial methodological expertise). The choice of vision-related quality of life measure was the NIH VFQ-25 questionnaire. This questionnaire was used in previous quality of life studies [21-23] showing significant reduction in quality of life for participants with hemianopia. In the absence of any vision-related quality of life measure specifically developed for stroke/vision research or clinical practice, the choice of VFQ-25 was appropriate, given its prior [21-23] and, of note, continued [24,25] use in research with stroke survivors with hemianopia. Indeed a recent systematic review of the evidence base for appropriate quality of life measures for stroke-related visual impairment, highlighted the VFQ-25 as one of very few instruments with potential in such trials [26]. Hepworth and colleagues [26] found no instruments that were developed specifically for visual impairment following stroke or which involved stroke survivors in the item identification phase of instrument development; they recommended further research to address this. Until such a stroke/vision specific questionnaire is developed, we believe that the VFQ-25 remains an appropriate choice of vision-related quality of life measure. A further advantage of choosing the VFQ-25 questionnaire was, because of its widespread use, comparisons can be made to other populations of visual impairment in the future. Bowers et al note the limited justification and discussion of all outcome measures. It was difficult within the word limit to provide justification and detailed explanations for every outcome measure. In recognition of this a separate results paper for our VFQ-25 data is being considered.

An important outcome measure to include in any intervention trial is adverse event rate. The VISION trial sought to ensure that these were reported specific to the time period when interventions were used (i.e. whilst wearing prism glasses or completing visual search training) highlighting a considerable difference between groups of 69% reported adverse events for the prism group and 7% for the visual search training group (0% for standard care). When planning the use of participant diaries, a key consideration was to ensure that participants could report their perceptions of intervention freely without clinician influence. We took specific care to ensure that participant diaries were completed at home and were reviewed only by independent blinded assessors.

A final aspect we should like to highlight is adherence to the CONSORT guidance when reporting trials. We followed the correct procedures of publishing our trial protocol [27] and ensured that the trial was conducted according to the pre-determined design. When publishing the final results of the trial, we adhered to CONSORT reporting guidelines and reported all the outcome measures stipulated in the protocol.

In conclusion, it is positive to see the emerging research for treatment of hemianopia since 2009. Clearly any new research planned for treatment of hemianopia should consider the current evidence base. The choice of outcome measures must be chosen wisely and we have highlighted in the VISION trial conclusions that alternative outcome measures should be considered if planning future clinical trials of multiple interventions for hemianopia. The evidence base will change and, consequently, when eventually reporting and interpreting results, this must be taken into consideration.

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